

Appln No. 10/039,952  
Amdt date March 23, 2005  
Reply to Office action of January 13, 2005

### REMARKS/ARGUMENTS

Claims 18-24 are pending in the application. In the Office action dated January 13, 2005, the Examiner requested clarification about the differences between this CIP application (10/039,952) and the parent application (09/702,421). Applicant hereby advises the Examiner that this CIP contains a Cross-Reference to Related Applications, a revised Summary of the Invention, a revised Detailed Description, and revised Claims, as well as a new Title. The revisions are readily seen in the "compare" copy that Applicant is submitting concurrently with this Amendment. Among other things, this CIP contains fourteen new examples (Nos. 29-42).

Also, in the latest Office action, the Examiner rejected claims 18-24 as being anticipated by each of the Jones patent publication and the May reference. Claim 25 was rejected as being obvious based on the combination of Jones and May in view of Mueller. Claims 18-25 were further rejected under 25 U.S.C. § 112, second paragraph as being indefinite. The title was objected to as being too generic. Applicant respectfully traverses the rejections and request reconsideration.

As noted above, Applicant has:

amended claim 18, line 1, by replacing "the production of" with --producing-- and by inserting a comma before the transition phrase "comprising";

amended claims 18 and 21, line 2, by deleting "the" before "reductive";

amended claims 22 and 24, line 2, by deleting "the" before "transamination"; and

cancelled claim 25.

Applicant has also amended the title to make it more descriptive of the invention recited in the pending claims. None of the amendments limit the scope of the invention in any way.

#### The Prior Art Rejections

Claims 18-24 stand rejected as being anticipated by each of the Jones and May references. Applicant respectfully traverses the rejection. Claims 18-24 describe a reaction in which a *ketone* is converted to an *amine*. The cited references have nothing to do with this.

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Jones teaches taking a serine hydrolase, such as subtilisin, replacing one or more amino acids by the specific amino acid cysteine, and chemically modifying the protein by alkylating the cysteine. In contrast, Applicant creates a mutated enzyme (by, e.g., modifying the DNA that encodes the protein, leading to random amino acid changes in the protein), which in turn leads to improved enzyme function for converting a ketone to an amine. The method of Jones also differs from the presently claimed invention in that Jones uses a *transacylation* reaction (i.e., a transamidation, transpeptidation, or transesterification), a class of reactions falling under the Enzyme Commission classification EC 3.4.-.-. In contrast, Applicant's claims 18-24 call for a reductive amination or transamination, in which a ketone is converted to an amine. This is a completely different class of reactions, falling under the Enzyme Commission classifications EC 1.5.-.- or EC 2.6.-.-. Nothing in the Jones disclosure would enable a skilled person to produce an amine by the conversion of a ketone. Nor is there any suggestion to adapt the methods of Jones to do so.

Similarly, the May reference is directed exclusively to the creation of a mutant hydantoinase (EC 3.5.2.2), a hydrolytic enzyme that catalyzes the hydrolysis of a hydantoin. This is also a completely different class of reaction from that recited in Applicant's pending claims. There is nothing in the May disclosure that would enable a person having ordinary skill in the art to produce an amine by the conversion of a ketone. Nor is there any suggestion to adapt the methods of May to do so.

Applicant's claims are thus clearly differentiated from both Jones and May. Independent claim 18, for example, recites:

A method for producing an amine from a target ketone, comprising:

creating a mutated enzyme that catalyzes reductive amination or transamination of the target ketone; and

providing the mutated enzyme in a reaction mixture comprising the target ketone under conditions sufficient to permit the formation of the amine to thereby produce the amine.

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Neither Jones nor May teach or suggest such a method, as neither reference discloses the conversion of a ketone to an amine.

Each of claims 19-24 depend, directly or indirectly from claim 18, and are submitted to be allowable as dependent upon an allowable base claim, and for the additional limitations recited therein.

The § 112 rejections

Applicant respectfully submits that the rejection of claims 18-24 based on a purported absence of an antecedent basis for various terms is overly formalistic and contrary to the common sense reading of the claims, which are understandable to any person having ordinary skill in the art. Nevertheless, to expedite prosecution, and without narrowing the scope of the claims in any way, Applicant has changed "the production of" to "producing" in claim 18, line 1, and further changed "the reductive" to "reductive" in reference to amination or transamination of the target ketone, in claims 18, 19, 21, 22, and 24.

The Examiner states that claim 18 does not recited any reacting or recovering steps. To the contrary, the last clause in the claim recites "providing the mutated enzyme in a reaction mixture comprising the target ketone under conditions sufficient to permit the formation of the amine *to thereby produce the amine*" (emphasis added). In other words, claim 18 specifies that a mutated enzyme is created and then provided in a reaction mixture that comprises the target ketone, under conditions sufficient to permit the formation of the amine, so that an amine is thereby produced. There is nothing indefinite about the claim.

The Examiner also states that claim 18 "is directed to a mutated enzyme but in what fashion or result the mutation is made is not seen in comparison with a not mutated enzyme." Applicant respectfully submits that the Examiner has not demonstrated any indefiniteness of the claim. Claim 18 is directed to a method for

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producing an amine from a target ketone, wherein one of the steps comprises creating a mutated enzyme that catalyzes reductive amination or transamination of the target ketone. Claim 18 can be read and readily understood by a person having ordinary skill in the art. Mutation techniques are identified generally at page 5 of the specification (i.e., mutagenesis, molecular breeding, gene reassembly), with particular examples provided at page 11, et seq. Such techniques do not need to be recited in claim 18 for the claim to be definite. In fact, claim 18 is *not* limited to a particular mutation technique. Nor is there a legal requirement that the claim make specific reference or comparison to a "not mutated enzyme."

The Examiner states that claim 19 "fails to further limit claim 18 from which it depends." Applicant respectfully disagrees. Line 2 of claim 18 recites "creating a mutated enzyme that catalyzes reductive amination *or transamination* of the target ketone" (emphasis added). In contrast, claim 19 specifies that the mutated enzyme catalyzes *reductive amination* of the target ketone. The two claims are not identical.

The Examiner also states that claim 20 (which depends from claim 19) "appears to be inconsistent where claim 18 from which claim 19 depends does not contain a dehydrogenase." Applicant respectfully disagrees that claim 20 is indefinite. At line 2, claim 18 calls for creating a mutated enzyme. Claim 19 specifies that the mutated enzyme catalyzes reductive amination of the target ketone. Claim 20 specifies that the mutated enzyme is an amino acid dehydrogenase. There is nothing inconsistent between claim 20 and claim 18. In the former, a mutated enzyme having the property of catalyzing reductive amination or transamination of a target ketone is specified. In claim 20, the mutated enzyme is more specifically characterized as an amino acid dehydrogenase, yet it still has to be capable of catalyzing a reductive amination of a target ketone.

Finally, the Examiner states that claim 21 "is not understood where one would not likely provide an enzyme that does not exist. Further, it is directed to mutating an enzyme but does not set forth how it is mutated." Applicant respectfully disagrees


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that the claim is indefinite. Claim 18 recites a method in which a mutated enzyme that catalyzes reductive amination or transamination of the target ketone is created and then provided in a reaction mixture . . . to produce the amine. Claim 21 calls for the additional limitation of first providing an existing enzyme, which is itself capable of catalyzing reductive amination of a ketone, and which is then mutated, wherein the mutated enzyme catalyzes reductive amination of the target ketone at a greater rate than the existing enzyme catalyzes reductive amination of the ketone. Claim 21 is both definite and consistent with claims 18 and 19. Further, although there is no legal requirement to specify how the enzyme is mutated, claim 21 specifies that "the mutated enzyme is created by mutating the existing enzyme". As noted above, mutation techniques are identified generally at page 5 of the specification (i.e., mutagenesis, molecular breeding, gene reassembly), with particular examples provided at page 11, et seq.

Accordingly, Applicant submits that this application is now in condition for allowance.

Respectfully submitted,

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